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## REVIEW

# Dalfampridine: Review on its recent development for symptomatic improvement in patients with multiple sclerosis



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**Abstract** Multiple sclerosis (MS) is a neurodegenerative disease of the central nervous system (CNS), causes irreversible disability in young adults but the cause and cure were unknown and it involves two arms: and causes demyelination and neurodegeneration. In the case of MS the massive activation of the immune system against putative CNS antigen leads to the loss of oligodendrocyte/myelin complex which slows down the impulse conduction in denuded axons. In demyelination diseases (e.g. MS) denuded axons frequently occur without axonal loss that is so characteristic of radiation injury. Since, the treatment strategies for MS have increased rapidly but still proper knowledge regarding the nature of MS cleared the way for several more specific, more effective, and more comfortable therapies. Here, because of the stimulating recent developments about oral treatment for MS, the current state of approved and future therapy options were summarized here. In particular, we highlight oral treatment options in MS and dalfampridine (4-aminopyridine) is an oral potassium channel blocker, which was recently approved by FDA (Food and Drug Administration) for symptomatic treatment of MS, it acts at the central and peripheral nervous systems, enhances conduction in demyelinated axons, and improves the walking ability of MS patients. Moreover number of clinical trials has evaluated the safety and efficacy of fampridine in MS

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patients and it represents a major advance in symptomatic therapy for MS. The objective of this manuscript is to provide an overview of the Chemistry, mechanism of action, pharmacodynamics, pharmacokinetics, preclinical and clinical studies, dosage and administration, side effects, contraindication, proper usage, and drug interaction of dalfampridine used in the treatment of MS patients.

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## 1. Introduction

Dalfampridine was approved by United State Food and Drug Administration (FDA) on January 22, 2010 and it is launched by Acorda therapeutics under the trade name AMPYRA which is used to improve walking in people suffering from multiple sclerosis (MS). The FDA granted dalfampridine orphan drug status, providing them 7 years of market exclusivity for the drug (Confavreux et al., 2000). The drug, a potassium channel blocker, was shown in clinical trials to improve walking speeds vs placebo and it acts by enhancing conduction in damaged nerves. Trouble with walking is one of the most debilitating problems of MS patients. The drug was previously known as fampridine sustained release with the proposed brand name Ampyra, but is now called dalfampridine (Rudick et al., 2010). Multiple sclerosis is a chronic disease that attacks the immune system and results in the degradation of nervous system functioning. MS is a disorder of the body's immune system that affects the central nervous system (CNS). Normally, nerve fibers carry electrical impulses through the spinal cord, providing communication between the brain, arms and legs. In people with MS, the fatty sheath that surrounds and insulates the nerve fibers called myelin deteriorates, causing nerve impulses to be slowed or stopped (Compston and Coles,

2008; Rosati, 2001). So, the person suffering from multiple sclerosis may experience periods of muscle weakness, loss of vision, loss of coordination, paralysis, spasticity, physical fatigue and decreased ability to think or remember. So, continuing in the advancement of clinical research and expansion of therapeutic options for people with MS, including treatments for the most debilitating symptoms and challenges associated with this disease, is critical to helping people with MS (Clanet, 2008; Compston and Coles, 2002; Ascherio and Munger, 2007; Lublin and Reingold, 1996). Fampridine has been used clinically in Lambert–Eaton myasthenic syndrome and multiple sclerosis. It acts by blocking potassium channels, prolonging action potentials and thereby increasing neurotransmitter release at the neuromuscular junction. The drug has been shown to reverse tetrodotoxin toxicity in animal experiments (Weinshenker, 1994; Pittock and Rodriguez, 2008). Fampridine has been shown to improve visual function and relieve fatigue in patients with multiple sclerosis (Judge and Bever, 2006). 4-AP is most effective in patients with the chronic progressive form of MS, in patients who are temperature sensitive, and in patients who have been suffering from MS for longer than 3 years. These periods of illness may become exacerbations and go into remissions. Fampridine-SR is an experimental drug that has been reported to possibly improve muscle

strength and walking ability for some people with MS (Wolswijk and Balesar, 2003). 4-Aminopyridine has a restricted use as an extremely effective bird poison sold under the brand name Avitrol, and may be dangerous to mammals and other animals. The most common target birds are pigeons, house sparrows, and starlings, if dosages are exceeded, compound forms of the active agent of sustained-release fampridine have been used in clinical practice for many years and are shown to improve walking ability in patients with multiple sclerosis. Clinical trials have now been completed that demonstrate effectiveness of the drug with statistical significance and a clinically meaningful end point. Approval of dalfampridine will enable patients to obtain a consistent exact dosage in a guaranteed time-released formula, and avoid the risk of getting an uncertain preparation from a compounding pharmacy with possible adverse effects (Vandiemen et al., 1993).

## 2. Chemistry

4-Aminopyridine (dalfampridine) is an organic compound with the chemical formula  $\text{H}_2\text{NC}_5\text{H}_4\text{N}$ . It is prepared by the decarboxylation of pyridine-4-carboxamide using sodium hypochlorite via Hoffman rearrangement. The pyridine carboxamide is generated from the corresponding nitrile, which in turn is obtained from the ammoxidation of 4-methylpyridine. The molecule is one of the three isomeric amines of pyridine. It is used primarily as a research tool, in characterizing subtypes of potassium channel, and has also been used to manage some of the symptoms of multiple sclerosis. The largest scale industrial application of 4-aminopyridine acts as a precursor to the drug pinacidil, which affects potassium ion channels. In the laboratory, 4-AP is a useful pharmacological tool in studying various potassium conductances in physiology and biophysics. It is a relatively selective blocker of members of Kv1 (family of voltage-activated  $\text{K}^+$  channels.). At concentration of 1 mM it selectively and reversibly inhibits shaker channels without significant effect on other sodium, calcium, and potassium conductances (Korenke et al., 2008).

## 3. Mechanism of action

Dalfampridine blocks tiny pores, or potassium channels, on the surface of nerve fibers, which may improve the conduction of nerve signals along nerve fibers whose insulating myelin coating has been damaged by MS, available in 10 mg tablet strength. It is a broad-spectrum potassium channel blocker that does not have a clinically important effect on duration of the QRS interval and it does not prolong the QTc interval, according to the FDA-approved for Ampyra. In animal studies, dalfampridine-mediated inhibition of potassium channels increased the conductivity of demyelinated nerve fibers. Electrophysiologic studies of demyelinated axons show that augmented potassium currents increase extracellular potassium ion concentration which decreases action potential duration and amplitude which may cause conduction failure. Potassium channel blockade reverses this effect. However, a recent study has shown that 4-AP is a potent calcium channel activator and can improve synaptic and neuromuscular function by directly acting on the calcium channel beta subunit ( $\beta_1$ ). MS patients treated with 4-AP exhibited a response rate of 29.5% to 80%. A long-term study (32 months) indicated that 80–90%

of patients who initially responded to 4-AP exhibited long-term benefits. Although improving symptoms, 4-AP does not inhibit the progression of MS. Spinal cord injury patients have also seen improvement with 4-AP therapy. These improvements include sensory, motor and pulmonary function, with a decrease in spasticity and pain (Zi-Zhen et al., 2009; Shrager, 1989; Chiu and Ritchie, 1980).

## 4. Pharmacodynamics

In Idiopathic unknown Pharmacodynamics, dalfampridine is a broad-spectrum voltage-gated potassium channel blocker, can increase action potential duration and amplitude, leading to improved demyelinated nerve fibers (loss of the myelin sheath insulating the nerves, and is the hallmark of some neurodegenerative autoimmune diseases, including multiple sclerosis, acute disseminated encephalomyelitis, transverse myelitis, chronic inflammatory demyelinating polyneuropathy, Guillain-Barré syndrome, central pontine myelinosis, inherited demyelinating diseases such as Leukodystrophy, and Charcot Marie Tooth) conduction and increase of neurotransmitter release at the synaptic ending. The metabolites have been shown to have no pharmacologic activity on potassium channels. Blocking voltage-gated potassium channels facilitates direct blocking of the synaptic and neuromuscular transmits ions conventionally and it was also suggested that fampridine can directly target presynaptic high voltage-activated calcium channels to potentiate neurotransmitter release independent of potassium channels. AMPYRA does not prolong the QTc interval and does not have a clinically important effect on QRS duration (Robert and Jeffrey, 2011; Peter et al., 2011).

## 5. Pharmacokinetics

Dalfampridine, a sustained-release oral preparation of fampridine, is rapidly absorbed, but relative bioavailability is 96% when compared to an aqueous oral solution. It gives a slower rise to a lower peak concentration  $C_{\text{max}}$  (term used in pharmacokinetics refers to the maximum concentration that a drug achieves in the tested area after the drug has been administered and prior to the administration of a second dose) i.e. 3–4 h post administration, with no effect on the extent of absorption AUC (area under curve). When dalfampridine is taken with food, there is a slight increase in  $C_{\text{max}}$  (12–17%) and a slight decrease in AUC (4–7%). Dalfampridine was nearly completely (95.5%) and rapidly eliminated within 24 h as unchanged drug via urinary excretion and 0.5% recovered in feces suggesting that it is unlikely to undergo substantial metabolic transformation with mean terminal disk position, half-life is 6.4 h and plasma half life of about 7.6 h in healthy individuals. Dalfampridine is largely unbound to plasma proteins (97–99%). The apparent volume of distribution is 2.6 L/kg. Two metabolites were identified: 3-Hydroxy-4-aminopyridine (4.3%) and 3-hydroxy-4-aminopyridine sulfate (2.6%). *In vitro* studies with human liver microsomes indicate that CYP2E1 was the major enzyme responsible for the 3-hydroxylation of dalfampridine. The identity of the CYP enzymes suspected of playing a minor role in the 3-hydroxylation of dalfampridine could not be established unequivocally (Vollmert and Henney, 2009; Judge et al., 2006; Bever and Judge, 2009; Oh et al., 2009; Chang et al., 1997; Uges et al., 1982).

## 6. Preclinical acute study

### 6.1. Carcinogenesis

Two year dietary carcinogenicity studies of dalfampridine were conducted in mice and rats. In mice, the doses tested (approximately 2, 12.5, and 80 mg/kg/day) were associated with plasma exposures (AUC) up to 18 times the plasma AUC in humans at the maximum recommended human dose (MRHD) of 20 mg/day. There was no evidence of drug-related carcinogenicity. In rats, the doses tested (approximately 2, 6, and 18 mg/kg/day) were approximately one, three, and nine times the MRHD on a body surface area (mg/m<sup>2</sup>) basis. There was a significant increase in uterine polyps at the highest dose tested.

### 6.2. Mutagenesis

Dalfampridine was negative in *in vitro* (bacterial reverse mutation, mouse lymphoma, and chromosomal aberration) and *in vivo* (mouse bone marrow, rat erythrocyte micronucleus) genetic toxicology assays.

### 6.3. Impairment of fertility

Oral administration of dalfampridine (doses of 1, 3, and 9 mg/kg/day) to male female rats prior to and throughout mating, and continuing in females up to day 13 of gestation or 21 of lactation resulted in no adverse effects on fertility. Reduced offspring viability and body weight were at 9 mg/kg/day. The mid dose (a no-effect dose) was similar to the MRHD on mg/m<sup>2</sup> basis (Stephen Krieger, 2011).

## 7. Clinical study

It was estimated that about 400,000 Americans were suffering from multiple sclerosis and 64–85% of patients will have difficulty in walking within 15 years of diagnosis. Dalfampridine is the first and only FDA-approved oral drug addressing walking impairment in patients with multiple sclerosis (Goodman et al., 2009; Johnson and Morgan, 2006).

### 7.1. Phase first

Single AMPYRA tablet 10 mg dose administered to healthy volunteers in a fasted state gave peak concentrations ranging from 17.3 ng/mL to 21.6 ng/mL occurring 3–4 h post-administration  $T_{max}$  (The amount of time that a drug is present at the maximum concentration in serum.). In comparison,  $C_{max}$  with the same 10 mg dose of dalfampridine in an oral solution was 42.7 ng/mL and occurred approximately 1.3 h after dosing. Exposure increased proportionally with dose. Common side effects include dizziness, nervousness and nausea, and incidence of adverse effects was shown to be less than 5% in all studies (Smith et al., 2010).

### 7.2. Phase second

In a phase II trial, percentage improvements in walking speed on the timed 25-foot walk test (primary endpoint) were not significant versus baseline or placebo during treatment with

dalfampridine ER 10, 15 or 20 mg twice daily. But according to a *post hoc*, response rates were significantly higher with dalfampridine ER than placebo, with a consistent mean improvement in walking speed of 25–29% seen in the pooled results from dalfampridine ER responders during the double-blind treatment period (Goodman et al., 2008). In placebo-controlled clinical trials of dalfampridine lasting up to 14 weeks duration, 4% of patients treated with dalfampridine had treatment emergent adverse events leading to discontinuations compared with 2% of placebo-treated patients. The treatment emergent adverse events led to discontinuation of at least two patients treated with dalfampridine and those that led to discontinuation more frequently compared with the placebo were headache (dalfampridine 0.5% vs placebo 0%), balance disorder (dalfampridine 0.5% vs placebo 0%), dizziness (dalfampridine 0.5% vs placebo 0%), and confusional state (dalfampridine 0.3% vs placebo 0%) (Goodman et al., 2002; Schwid et al., 1997).

### 7.3. Phase third

Allocation: randomized, Control: Placebo control, Endpoint classification: Safety/efficacy study, Intervention model: parallel assignment, Masking: double blind (subject, caregiver, investigator, and outcomes assessor), Primary purpose: treatment. In two phase III clinical trials, a significantly greater proportion of people on therapy had a consistent improvement in walking speed compared to those in the placebo group. In the first trial, involving 301 people with any type of MS, walking speed increased by 25% compared with the placebo (Goodman et al., 2009). Results from the second phase III study, involving 240 people with MS, confirmed the benefits seen in the first trial. Among those taking dalfampridine who improved in walking speed, there was also a statistically significant improvement in leg strength. AMPYRA has been evaluated in a total of 1952 subjects, including 917 MS patients. A total of 741 patients have been treated with AMPYRA for over 6 months, 501 for over 1 year and 352 for over 2 years (Goodman et al., 2007). The experience in open-label clinical trials is consistent with the safety profile observed in the placebo-controlled clinical trials. As in controlled clinical trials, a dose-dependent increase in the incidence of seizures has been observed in open-label clinical trials with AMPYRA in patients with MS as follows: AMPYRA 10 mg twice daily 0.41 per 100 person-years; dalfampridine 15 mg twice daily 1.7 per 100 person-years. Trial 1 was a randomized, placebo-controlled, parallel group, 21-week study (1 week post screening, 2-week, single-blind placebo run-in, 14-week double-blind treatment, and 4-week no treatment follow-up) in 301 patients with multiple sclerosis at 33 centers in the U.S. and Canada: 229 patients assigned to AMPYRA 10 mg twice daily and 72 patients assigned to placebo. A total of 283 patients (212 AMPYRA and 71 placebo) completed all study visits. Patient inclusion criteria included the ability to walk 25 feet in 8–45 s. Patient exclusion criteria included a history of seizures or evidence of epileptic form activity on a screening EEG, and onset of an MS exacerbation within 60 days (Goodman et al., 2010).

### 7.4. Trial one

This randomized, placebo-controlled, parallel group, 21-week study enrolled 301 patients with multiple sclerosis at 33 centers



in the U.S. and Canada. The patients were assigned to Ampyra 10 mg twice daily or placebo. A total of 283 subjects completed the study. The primary measure of efficacy was walking speed (in feet per second) as measured by the Timed 25-foot Walk (T25W), using a responder analysis. A significantly greater proportion of patients taking Ampyra were responders compared to patients taking placebo: 34.8% vs 8.3%, respectively. The increased response rate was observed across all four major types of MS disease course (Goodman et al., 2007, 2009, 2010). During the double-blind treatment period, a significantly greater proportion of patients taking Ampyra 10 mg twice daily had increases in walking speed of at least 10%, 20%, or 30% from baseline, compared to placebo.

### 7.5. Trial two

This randomized, placebo-controlled, parallel group, 14-week study enrolled 239 patients with multiple sclerosis at 39 centers in the U.S. and Canada. The subjects were assigned to 10 mg twice daily and or placebo. A total of 227 patients completed the study. The primary endpoint was walking speed (in feet per second) as was measured by the Timed 25-foot Walk (T25W), using a responder analysis. A significantly greater proportion of patients taking Ampyra were responders compared to patients taking placebo: 42.9% vs 9.3%, respectively. The increased response rate was observed across all four major types of MS disease course. During the double-blind treatment period, a significantly greater proportion of patients taking Ampyra 10 mg twice daily had increases in walking speed of at least 10%, 20%, or 30% from baseline, compared to the placebo. In Trial 1 and Trial 2, consistent improvements in walking speed were shown to be associated with improvements on a patient self-assessment of ambulatory disability, the 12-item Multiple Sclerosis Walking Scale (MSWS-12), for both drug and placebo treated patients. However, a drug-placebo difference was not established for that outcome measure. The majority of patients in these trials (63%) were using immunomodulatory drugs (interferons, glatiramer acetate, or natalizumab), but the magnitude of improvement in walking ability was independent of concomitant treatment with these drugs. No differences in effectiveness based on degree of impairment, age, gender, or body mass index were detected. There were too few non-Caucasians in the patient population to evaluate the effect of race (Goodman et al., 2007, 2009, 2010).

## 8. Dosage and administration

The maximum recommended dose of AMPYRA is one 10 mg tablet twice daily, taken with or without food. Doses should be taken approximately 12 h apart. Patients should not take double or extra doses if a dose is missed. No additional benefit was demonstrated at doses greater than 10 mg twice daily and adverse reactions and discontinuations were more frequent at higher doses. Tablets should only be taken whole; do not divide, crush, chew, or dissolve. AMPYRA is contraindicated in patients with moderate or severe renal impairment. The seizures in patients with mild renal impairment (CrCl 51–80 mL/min) is unknown, but AMPYRA is contraindicated in patients with moderate or severe renal impairment. The risk of seizures in patients with mild renal impairment (CrCl 51–80 mL/min) is

unknown, but AMPYRA plasma exposure in these patients may approach that seen at a dose of 15 mg twice daily dose that may be associated with an increased risk of seizures; estimated CrCl should be known before initiating treatment with AMPYRA (Lawrence and Andrew, 2011).

### 8.1. Side effects

Urinary tract infection was the most common adverse event associated with dalfampridine during clinical trials. Given at doses greater than the recommended 10 mg twice a day, dalfampridine can cause seizures, balance disorder, swelling in the nose or throat, constipation, diarrhea, indigestion, throat pain, and burning, tingling, itching of skin, insomnia, dizziness, headache, nausea, asthenia, back pain, balance disorder, multiple sclerosis relapse, paresthesia, nasopharyngitis, constipation, dyspepsia, pharyngolaryngeal pain, problems with balance, MS relapse, burning, tingling or itching of the skin, irritation of the nose and throat, constipation, indigestion and throat pain (Pickett and Enns, 1996; Johnson and Morgan, 2006).

## 9. Contraindication

Dalfampridine is contraindicated in patients with moderate to severe kidney disease because the blood levels with the drug approach those associated with the occurrence of seizures. Because of concern for this adverse event, dalfampridine is contraindicated in patients with a prior history of seizure and should be discontinued in patients in which seizure occurs. Dalfampridine should not be consumed by pregnant women, children less than 18 years of age and it should not be taken with other aminopyridine medications. Dalfampridine demonstrated efficacy in all four major types of MS, including relapsing-remitting, secondary progressive, progressive relapsing, and primary progressive, and can be used alone or in combination with immunomodulatory drugs (Smith et al., 2010; Peter et al., 2011).

### 9.1. Proper usage

Dalfampridine should be kept out of the reach of children and should not take more than two tablets in a 24-h period. The medication can be taken with or without food but it should never chewed and crushed before swallowing because it may cause the medication to release too quickly, which may increase the risk of having a seizure. Suppose if a dose of dalfampridine is missed then never stop the therapy but continue with the next dose at your regular scheduled time (Schapiro et al., 2010).

### 9.2. Specific populations

The safety and effectiveness of AMPYRA in patients younger than 18 years of age have not been established. It is known to be substantially excreted by the kidney and the risk of adverse reactions including seizures increases with the exposure to dalfampridine. Because elderly patients are more likely to have decreased renal function, it is particularly important to know the estimated creatinine clearance (CrCl) in these patients. A population pharmacokinetic analysis suggested that female

patients would be expected to have higher maximum dalfampridine plasma concentration ( $C_{\max}$ ) than male patients. The pharmacokinetics of dalfampridine was studied in nine male and 11 female subjects with varying degrees of renal function. Total blood clearance of dalfampridine was reduced by about 45% in patients with mild renal impairment (CrCl 51–80 mL/min), by about 50% in patients with moderate renal impairment (CrCl 30–50 mL/min), and by about 75% in patients with severe renal impairment (CrCl < 30 mL/min). The terminal half-life of dalfampridine is about 3.3 times longer in patients with severe renal impairment but is not prolonged in patients with mild or moderate renal impairment. Since dalfampridine is primarily excreted unchanged in urine, hepatic impairment is not expected to significantly affect dalfampridine pharmacokinetics or recommended dosing. AMPYRA should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus. No evidence of developmental toxicity was found in either species at the highest doses tested, which were maternally toxic. Oral administration of dalfampridine (at doses of 1, 3, and 9/6 mg/kg/day; high dose reduced during the second week of dosing) to rats throughout the pregnancy and lactation periods resulted in decreased offspring survival and growth (Goodman et al., 2007, 2009, 2010). The no-effect dose for pre- and postnatal developmental toxicity in rats (1 mg/kg) is approximately 0.5 times the MRHD on mg/m<sup>2</sup> basis.

### 9.3. Drug interactions

Dalfampridine kinetics was not affected by co-administration of subcutaneous injections of eight million unit's interferon beta-1b. No pharmacokinetic drug–drug interaction was observed with co-administration of dalfampridine 15 mg and baclofen 10 mg. *In vitro* data with human liver microsomes showed that dalfampridine was not a direct or time-dependent inhibitor of CYP1A2, CYP2A6, CYP2B6, CYP2C8, CYP2C9, CYP2C19, CYP2D6, or CYP3A4/5. Dalfampridine is not likely to affect the pharmacokinetics of drugs that are substrates of these enzymes. Other *in vitro* studies with cultured human hepatocytes with dalfampridine had little or no effect on CYP1A2, CYP2B6, CYP2C9, CYP2C19, CYP2E1 or CYP3A4/5 enzyme activities. Consequently, the potential for dalfampridine to induce human hepatocytes at therapeutic concentrations is remote. *In vitro*, dalfampridine is not a substrate or an inhibitor for the p-glycoprotein transporter (Goodman et al., 2010; Goodman et al., 2009; Goodman et al., 2007). The pharmacokinetics of AMPYRA is unlikely to be affected by drugs that inhibit the p-glycoprotein transporter, and dalfampridine is not likely to affect the pharmacokinetic of drugs that are substrates of the p-glycoprotein transporter.

## 10. FDA approval and market authorization

On January 30, 2009 Acorda Therapeutics, announced the submission of a new drug application to the U.S. (FDA) for Fampridine-SR. Fampridine-SR was accepted by the FDA on May 5, 2009. The FDA set a prescription drug user fee act (PDUFA) on October 22, 2009; the PDUFA date is the target date for the FDA to complete its review. On May 6, 2009 acorda therapeutics, announced that the U.S. (FDA)

has accepted the Fampridine-SR New Drug Application (NDA) for filing, assigning priority review and on Aug 25, 2009 Acorda Therapeutics, announced that the U.S. (FDA) has confirmed that its Peripheral and Central Nervous System Drugs Advisory Committee will review the Company's New Drug Application (NDA) for Fampridine-SR on October 14, 2009 and Acorda submitted additional information on its proposed Risk Evaluation and Mitigation Strategy (REMS) program. The Company also announced that it has received preliminary approval for the proposed trade name Amaya from the FDA. On 12 January 2010, Biogen Idec announced that the submission of a Marketing Authorization Application (MAA) to the European Medicines Agency for prolonged release fampridine tablets helpful in the walking ability of adult patients suffering from multiple sclerosis. The US FDA accepted this submission as a solicited major amendment to the Fampridine-SR NDA. FDA approved dalfampridine in patients with multiple sclerosis on January 22, 2010. Biogen Idec will commercialize fampridine as a prolonged release tablet in markets outside the U.S.

## 11. Conclusion

In the case of multiple sclerosis there is conduction abnormality, including conduction delay or block due to the loss of the oligodendrocyte myelin complex which in turn results in the reorganization of axolemmal ion channels. So, the agents which block potassium channels have been investigated in the context of clinical trials with positive impact on impulse conduction in experimentally-induced demyelination in MS patients. Dalfampridine is an extended release form of fampridine (4-aminopyridine), which has been recently been approved by the US FDA for symptomatic treatment of MS patients. While this new oral blocker of voltage-gated potassium channels does not have any impact on the underlying pathology of MS, it has been demonstrated to improve fatigue and walking ability in these patients.

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